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wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease and autoimmune hepatitis.

REMARKS

Of pending claims 4, 6-7, and 9-17, claims 4 and 14 are rewritten. Claims 15 and 17 have been cancelled. Claims 7 and 9-13 have been withdrawn. With this response, claims 4, 6-7, 9-14, and 16 remain pending.

Applicant does not believe that any fees are due at this time; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to this document, the Commissioner is authorized to deduct the fees from Howrey Simon Arnold & White, LLP Deposit Account No. 01-2508/13240.0004.NPUS00/BNT.

For the Examiner's convenience, a list of currently pending claims is attached at the end of this document.

I. Rejection under 35 U.S.C. § 112, first paragraph

Claims 4, 6, and 14-15 were rejected under 35 U.S.C. § 112, first paragraph. Allegedly, the specification, while being enabling for the use of human, porcine, bovine, and rat HMG for the binding of autoantibodies in human SLE, Sjogrens syndrome, Behcet's disease, scleroderma, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Crohn's disease, and autoimmune hepatitis, does not reasonably provide enablement for the use of any HMG-1 or HMG-2 family protein.

Applicant respectfully disagrees. The specification does provide sufficient guidance for a skilled artisan to obtain a polypeptide having an amino acid sequence homology of at least 90% with human HMG-1 (SEQ ID NO:1), or a fragment thereof which reacts with an antibody from an autoimmune patient. The specification also provides sufficient guidance for a skilled artisan to obtain a polypeptide having an amino acid sequence homology of at least 80% with human HMG-2 (SEQ ID NO:2), or a fragment thereof which reacts with an antibody from an autoimmune patient.

For example, the specification at page 12, line1 through page 13, line 5 describes how to obtain a polypeptide of the HMG-1 or HMG-2 family, or a derivative sequence thereof having a deletion, substitution, or addition of one or more amino acids. At page 10 line 32 through page 11, line 16, the specification provides a polypeptide belonging to the HMG-1 or HMG-2 family, based on an amino acid sequence homology. On page 11, last paragraph, the specification describes how to prepare and how to determine whether a fragment of HMG-1 or HMG-2 reacts with an antibody from an autoimmune disease patient, and provides examples of this determination. Claims 4 and 14, as amended, exclude polypeptides and polypeptide fragments of HMG-1 or HMG-2 which do not react with an antibody from an autoimmune disease patient.

Applicant submits a declaration by Fumio Osakada indicating that fragments of HMG-1 or HMG-2 react with sera obtained from an autoimmune disease patient, and that these fragments can be used for diagnosing autoimmune disease.

Furthermore, Applicant points out that there is a sequence homology of 79% between HMG-1 and HMG-2, and that both peptides react with sera obtained from an autoimmune disease patient. Accordingly, a polypeptide having an amino acid sequence homology of 90% or

more with HMG-1, or a polypeptide having an amino acid sequence homology of 80% or more with HMG-2 can react with an antibody from an autoimmune disease patient.

Applicant respectfully requests that the rejections of claims 4, 6, and 14-15 under 35 U.S.C. § 112, first paragraph be withdrawn.

II. Rejection under 35 U.S.C. § 102

Claims 14-17 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ayer et al. (*Arthritis & Rheumatism*, 37(1): 98-103, 1994; hereinafter "Ayer"). The Examiner stated that Ayer teaches bovine HMG-1 or -2, wherein the HMG protein binds antibodies of a scleroderma disease patient. Claims 15 and 17 have been cancelled in an effort to expedite prosecution.

For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 677, 7 U.S.P.Q.2d 1315, 1317 (Fed. Cir. 1988).

Ayer presents the binding of bovine HMG-1 and HMG-2 to antibodies from a scleroderma disease patient. Ayer does not teach the binding of the claimed HMG-1 or HMG-2 polypeptide sequences to antibodies obtained from an autoimmune disease patient, wherein the disease is rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease, or autoimmune hepatitis.

Applicant respectfully requests that the rejections of claims 14 and 16 under 35 U.S.C. § 102 be withdrawn.

III. Rejection under 35 U.S.C. § 103

Claims 4 and 6 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ayer.

According to MPEP § 706.02(j), for a claim to be obvious, there must be a) a suggestion or motivation to combine reference teachings, b) a reasonable expectation of success, and c) the references must teach all of the claim limitations, *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Ayer offers the binding of bovine HMG-1 and HMG-2 to antibodies obtained from a scleroderma disease patient. There is no teaching or suggestion that the HMG-1 and HMG-2 polypeptides described in the pending claims could bind to antibodies obtained from an autoimmune disease patient, wherein the disease is rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease, or autoimmune hepatitis.

Accordingly, Applicant requests that the rejections of claims 4 and 6 under 35 U.S.C. § 103 be withdrawn.

In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding objections and rejections are respectfully requested. All amendments are made in a good faith effort to advance the prosecution on the merits. Applicant respectfully submits that no amendments have been made to the pending claims for the purpose of overcoming any prior art rejections that would restrict the literal scope of the claims or equivalents thereof. Applicant reserves the right to subsequently take up prosecution of the claims originally filed in this application in continuation, continuation-in-part, and/or divisional applications.

The Examiner is encouraged to call the undersigned should any further action be required for allowance.

Respectfully submitted,

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Marked up version of rewritten claims amended in this Response

4. (Three Times Amended) A kit for diagnosing an autoimmune disease, the kit comprising:

a first antigen comprising a human HMG-1 polypeptide, a polypeptide having an amino acid sequence homology of 90% or more with human HMG-1 indicated by SEQ ID NO:1, or a fragment thereof which reacts with an antibody from an autoimmune disease patient [polypeptide from an HMG-1 family or a fragment of a polypeptide from the HMG-1 family];

a second antigen comprising a human HMG-2 polypeptide, a polypeptide having an amino acid sequence homology of 80% or more with human HMG-2 indicated by SEQ ID NO:2, or a fragment thereof which reacts with an antibody from an autoimmune disease patient [polypeptide from an HMG-2 family or a fragment of a polypeptide from the HMG-2 family];

a first component for detecting a first antigen-antibody complex; and

a second component for detecting a second antigen-antibody complex; wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, [scleroderma,] primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease and autoimmune hepatitis.

14. (Amended) A diagnostic drug for detecting an antibody of autoimmune diseases, wherein: the drug comprises:

a human HMG-1 polypeptide, a polypeptide having an amino acid sequence homology of 90% or more with human HMG-1 indicated by SEQ ID NO:1, or a fragment thereof which reacts with an antibody from an autoimmune disease patient [polypeptide selected from an HMG-1 family]; or

a human HMG-2 polypeptide, a polypeptide having an amino acid sequence homology of 80% or more with human HMG-2 indicated by SEQ ID NO:2, or a fragment thereof which reacts with an antibody from an autoimmune disease patient [polypeptide selected from an HMG-2 family];

[a fragment of a polypeptide selected from an HMG-1 family; or

a fragment of a polypeptide selected from an HMG-2 family;]

the drug reacts with an antibody of an autoimmune disease patient; and

wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, human systemic lupus erythematosus, Sjögren's syndrome, Behçet's disease, primary biliary cirrhosis, microscopic polyangitis/polyarteritis nodosa, ulcerative colitis, Chrohn's disease and autoimmune hepatitis [the autoimmune disease is not ulcerative colitis when the polypeptide or fragment is a neutrophil 28 kDa antigen].